

REMARKS

Claims 24-39 are pending in the present application. Applicant notes with appreciation that the rejection of claims under 35 U.S.C. §112, first paragraph and 35 U.S.C. §102(b) over Olsen have been withdrawn by the Office. New grounds of rejection have been made, however.

Claims 24-33 are rejected under 35 U.S.C. §112, second paragraph, as indefinite. The Office Action specifies that claims 24 and 31 are confusing due to the recitation: "loading particles with the solution without adversely influencing the function of the conjugates by displacing the biomolecules by the detergent or by interactions of the biomolecules or the colloidal particles with the detergent after loading." The rejection appears to be based on confusion as to displacement of the biomolecules adsorbed on the particles by the detergent in the solution.

Applicant has amended claims 24, 31 and 34 to avoid use of the assertedly confusing language and to make clear the respective influences and relationships referenced in the claim. Applicant respectfully submits that the amended language makes clear that the detergent present in the biomolecule coating solution does not adversely influence the function of the conjugates by displacing the biomolecules from adsorption onto the particles or by interacting with the biomolecules or the particles after loading. Thus, the invention more clearly relates to a process whereby biomolecules can be coated onto particles without detergent occupying space on the particles that otherwise might be occupied by biomolecules or competing for adsorption with the biomolecules. Therefore, displacement of biomolecules on the particles after coating does not take place such that the ability of the particle

to function as a biomolecule-coated particle is adversely affected.

Applicant believes that these amendment to phraseology do not change the scope of the claims and submit that the claims now fully comply with the standards of 35 U.S.C. §112, second paragraph. Applicant therefore respectfully requests that the rejection for reasons of indefiniteness be withdrawn.

Claims 24, 30, 31 and 33 are rejected under 35 U.S.C. §102(e) as anticipated by Liberti et al. The Office Action states that Liberti et al. teach a coating process for coating a wide range of materials onto colloidal magnetically responsive particles to obtain stable microagglomerates, including steps of mixing the particulate and coating materials subdividing the particles, permitting coating and recovering resuspended, coated particles. The Office did not find persuasive previous arguments that Liberti et al. fails to teach biomolecule-coated particles that do not have adversely influenced function as required by the claims of this application. The Office Action states that Liberti et al. inherently teach this since the Liberti et al. particles are "stabilized" and therefore not "adversely influenced."

Applicant traverses the rejection of these claims as anticipated by Liberti et al. and submits that the cited teachings do not provide a sufficient basis to anticipate the present claims. To make out a case for anticipation, the Office must show that the cited reference contains, within its four corners, each and every claim limitation of the rejected claim. M.P.E.P. §2131. Liberti et al. describe a method for producing magnetically responsive particles that are coated with a wide range of materials, including detergents, and that are "stable." The particles are described as having a stabilizing coating (col. 4, lines 59-60) which is selected for its ability to allow coated particles that have agglomerated to be separated and resuspended (col. 5, lines 4-6,

39-43). Liberti et al. emphasize that it is important to select a coating material that produces a coating that remains intact when the coating particles are removed from suspension in order to produce a resuspendable coated particle product in distinguishing their invention from the prior art (col. 6, lines 6-10). Thus the Liberti et al. methods are designed to produce a coating (including specifically a detergent coating when the coating material is detergent) that allows coated but agglomerated materials to be resuspendable by chemical or preferably by mechanical means, such as sonication. ["Stability" of these particles refers to the stability of the suspendability of the particles and not to the function of the particle]

The methods of this invention, on the other hand, are directed to producing particles coated with biomolecules, not detergent, notwithstanding that the biomolecule coating solution contains detergent. In the coated particles here, detergent does not coat the particle so that surface space on the particle, taken up by adsorbed or coated detergent, is no longer available for stable adsorption of biomolecules, thus resulting in a particle with fewer biomolecules on the surface. In such a particle, the detergent coating would adversely influence the function of the conjugate because biomolecules are displaced on the surface by detergent. The adversely-affected function referred to is the function of the biomolecule-coated particle due to lower concentration of functional molecules in the particle. This aspect of the invention is made clear by the amendments to the claims discussed above and by the description throughout the specification, which describes stabilized particles in which the detergent in the coating solution does not impair binding of the functional biomolecule to the extent found in the prior art. See, for example, page 5, last paragraph.

The specification also discusses other favorable properties of the inventive particles, which have a lower aggregation tendency in solution (page 6, first full paragraph) and yet do not have adversely affected conjugate function due to displacement of biomolecules by detergent (page 6, second full paragraph). The Liberti et al. particles are designed to agglomerate, but be resuspendable due to the presence of the coating, including detergent coating. On the other hand, the particles of this invention do not aggregate to the extent of prior art particles and have a coating of biomolecules that is not displaced from the surface by detergent.

Liberti et al. does not disclose the particles of this invention. By focusing on a perceived lack of "adverse influence" by the detergent coating on the Liberti et al. particles, the Office is missing a major distinction between the invention here and the disclosures of Liberti et al. The detergent of Liberti et al. does not "adversely influence" the coating of the Liberti et al. particles' stability because the "stability" referred to by Liberti et al. is stability "at reduced particle size," which allows the particles to be resuspendable. See Liberti et al., col. 5, lines 2-6. The authors of Liberti et al. produced particles which form a stable suspension, therefore, and did not concern themselves with producing particles wherein the detergent does not adversely influence the function of the conjugate as the claims here require. Thus, Liberti et al. do not teach or even suggest that a particle can be produced which is "stabilized," as to suspendability but also has unimpaired function resulting from coating with detergent. Liberti et al. therefore fails to teach this claim limitation and cannot anticipate the claims of this application.

In summary, Liberti et al. do not teach or suggest a particle wherein the detergent present in a coating solution does not adversely affect biofunction of the particles produced, and in fact did not even recognize this possibility. Liberti et al. do not provide a method for avoiding adverse influence of detergent in the solution, only a method for stabilizing the suspendability of the particles.

Applicant therefore respectfully submits that Liberti et al. cannot form a proper basis for a rejection under 35 U.S.C. §102(e) and requests that the Office withdraw the rejection.

Claims 25-29, 32 and 34-39 are rejected under 35 U.S.C. §103(a) as unpatentable over Liberti et al. in view of Nichtl et al. Applicant has discussed the disclosures of Liberti et al. and the failure of these disclosures to teach or suggest each and every element of the claims in this application above. These discussions apply equally well to this rejection, therefore Applicant refers the Office to the discussions above concerning anticipation of claims of Liberti et al.

Nichtl is cited for teaching use of a stabilizer to minimize aggregation of particles and to saturate free surfaces on the particles. This teaching does not make up for the lack of disclosure in Liberti et al. concerning use of detergent which does not adversely influence conjugate function by displacing biomolecules from the particle surface or by interacting with the biomolecule or the particle. Nichtl teaches that stabilizers of the prior art, including detergents, bind adsorptively to free surfaces of metal particles, see col. 1, lines 46-64, and proposes using polyethylene glycol stabilizer to avoid the problems of the prior art. Nichtl therefore teaches away from using detergents in biomolecule-particle conjugates as the present claims require. An additive to biomolecule coating solutions that binds to free

surfaces of the particles to be coated with the biomolecules would be expected to interfere with the binding of biomolecules to the particle surface. Nichtl proposes to avoid detergent as a stabilizer. The present invention, however, is based on the surprising discovery that particles according to the this invention do not suffer from this drawback recognized in the prior art and alluded to by Nichtl.

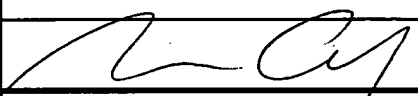
Liberti et al. fail to teach or even suggest a particle according to this invention wherein detergent does not adversely affect the function of biomolecule-coated particles when present in the coating solution. Nichtl teaches that detergent stabilizers bind to particles' free surfaces, and recommends a different method for stabilizing particles. Therefore, the person of skill would not view these two references as combinable. Further, even if the references were combined, the combination of these two references discloses, at most, a particle which forms a stable suspension due to the presence of detergent, but in which detergent competes with biomolecule for binding to the particle, thereby potentially adversely influencing the particle function by interacting with the colloidal particles.

To make out a prima facie case of obviousness, the Office must meet three criteria. The cited prior art references must teach or suggest each and every claim limitation, the prior art must contain a suggestion or motivation to modify the cited reference to achieve the invention of the rejected claims, and there must be a reasonable expectation of success. M.P.E.P. §2143. The Office cannot make out a prima facie case of obviousness based on the cited references. First, they do not disclose or even suggest a particle coated using a detergent-containing solution in which the detergent does not adversely influence the function of the biomolecule-particle conjugates. Second, there can be no

motivation to combine and modify these teachings to achieve such a particle because Nichtl teaches away from using detergent in biomolecule coating solutions because it interacts with the colloidal particles. See M.P.E.P. §2145(X)(D)(2). The inventors here also have proceeded against the conventional and accepted wisdom in the art, as discussed in Nichtl, a clear indication of nonobviousness, see M.P.E.P. §2145(X)(D)(3), and clear evidence that there is no reasonable expectation of success.

For the forgoing reasons, Applicant submits that the Office has not and cannot make out a case of prima facie obviousness as to the claims rejected here. Applicants request the rejection under 35 U.S.C. §103(a) be withdrawn.

Applicants believes that the claims are in condition for allowance and request favorable consideration at this time.

RESPECTFULLY SUBMITTED,					
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